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Summary of Presentations at Plenary Sessions and Dissussion Workshop at Twenty-First National Meeting of the Reticuloendothelial Society

Montreal, Canada, October 14-17, 1984

Grant #N00014-84-G-0190

Final Report

The meeting was initiated by a discussion workshop on Cellular and Molecular Biology of Gamma Interferon, chaired by Drs. Robert Schreiber and Ed Havell. The first presentation was by Dr. Havell who provided a detailed overview on the background about the development and characterization of gamma interferon. He considered the possible differences between natural and recombinant gamma interferon and discussed the broad range of their biologic effects. He described antibodies which he has developed against gamma interferon which have been very helpful to dissect out the level of gamma interferon in a variety of biologic systems. The next presentation was by Dr. Patrick Grey from Genentech, who summarized ~~information~~ about the genetic engineering of mouse and human gamma interferon. ~~He also~~ presented information about ~~the more recent~~ cloning of the genes for human lymphotoxin and tumor necrosis factor. The next presentation was by Dr. Robert Schreiber, who discussed the relationship between mouse interferon and macrophage activating factor. He presented a series of arguments supporting the hypothesis that gamma interferon may be the main, if not the only macrophage activating factor. The final presentation in the workshop was by Dr. Tom Hamilton, who has been studying the interacellular effects induced by mouse gamma interferon. He described the effects on activation of protein kinase C, as well as on other metabolic pathways.

RETICULOENDOTHELIAL SOCIETY

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February 14, 1985

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RE: Grant N00014-84-G-0190
Final Report

Gentlemen:

As requested, I am enclosing a copy of the final report for grant #N00014-84-G-0190.

Sherwood M. Reichard
Executive Director

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Enclosures

The keynote address for the annual meeting was presented by Dr. Joseph Goldstein, who has been a pioneer in studies on serum glycoproteins and their role in atherosclerosis. He presented a detailed and kind of overview of the major contribution of low density glycoproteins as transport mechanisms for cholesterol and the key role which they play in induction of atherosclerosis. He described the structure of the low density lipoproteins in the cellular receptors for these proteins and how the levels of both the circulating type of proteins and the receptors are regulated. He presented fascinating recent information about various genetic defects which are providing new insights into the defects contributing to heart disease. Although the detailed information which he presented is somewhat distant from the immediate concerns of the Reticuloendothelial Society, he drew a series of analogies between the information accumulated in his systems with the receptor-cytokine interactions which are directly related to the concerns of the Society.

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The first plenary session of the meeting was on Cell-Cell Interaction: A Basic Host Recognition System. The first presentation was by Dr. Luis Glaser from Washington University, who spoke on the role of cell-cell recognition in cell growth and differentiation. His emphasis was on cell surface structures involved in interaction among various cell types, the signals which this recognition induces, and how this leads to regulation of cell differentiation. The next talk was by Dr. Ronald Schnaar, who spoke on Cell Surface Carbohydrates in Cellular Recognition and Response. He emphasized the characteristics of a variety of carbohydrates on the

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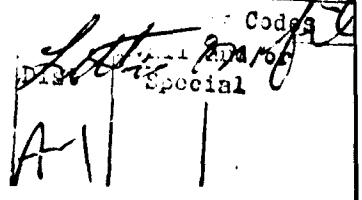

cell surface and how these related to receptor mediated recognition events and the induction of a variety of functional changes in cells. The next talk was by Dr. Dolph Adams who spoke on Selective Capture of Tumor Cells by Macrophages: Cell Biology and Regulation. Dr. Adams described the rather selective interactions between activated macrophages and most tumor cells, with high affinity binding of tumor cells only to activated marcophages. He described the various stages of activation of macrophages and summarized the current knowledge about the events leading to cytotoxicity by activated macrophages. The last talk in this session was by Dr. C. Garrison Fathman, who spoke on MHC Restriction in T-Cell Activation by Antigen Presenting Cells. He presented a detailed summary of the key role of the major histocompatability complex in the activation of T-cells and discussed the mechanisms by which MHC determinants are handled by antigen-presenting cells, like macrophages, and how the combination of MHC determinants and specific antigens are involved in recognition and activation of T-cells.

The second plenary session was on Recent Advances in Neutrophil Biology. The first presentation was by Dr. James Niedel, who spoke on the Role of Phorbol Ester Receptor-Protein Kinase C in Myeloid Maturation. He presented information indicating that phorbol esters are bound to specific receptors on myelomonocytic cells and that binding of phorbol esters to such receptors stimulate the activation of protein kinase-C, with resultant phosphorylation of several cellular proteins. This mechanism seems to have

physiologic importance, since some of the functional changes in myeloid monocytic differentiation can be mimicked by the addition of diacyl glycerol to cells, which also activates the protein kinase C.

The next presentation was by Dr. John Gallin, who spoke on Modulation of Neutrophil Responses to Chemoattractants. He discussed the receptors for the formylated peptide, f-met-leu-phe and how this chemoattractant and complement components can influence the functions of neutrophils. The next presentation was by Dr. Douglas Fearson, who spoke about the Neutrophil C3B Receptor: Modulation and Function. He summarized information about characteristics of this receptor and how it interacts with the third component of complement, and the functional changes in neutrophils that are induced by this interaction. The final presentation in this session was by Dr. Eric Brown, who spoke about Fibronectin and Neutrophil Function. Fibronectin has been clearly shown to be a key protein for adherence of cells like neutrophils and for stimulation of some of their functional activities.

The last plenary session in the meeting was on Human Macrophages and Disease. This summarized a series of interesting information about the involvement of macrophages in several major diseases. The first presentation was by Dr. Peter Henson, who summarized information about the role of macrophages in various human and inflammatory diseases. The next presentation was by Dr. Steve Krane, who summarized the key role played by macrophages in the development of various forms of arthritides.

The next presentation was by Dr. Russell Ross, who summarized information about the involvement of macrophages in atherosclerosis. Accumulation of macrophages in a prominent feature of atheromas and their ingestion of cholesterol and other lipids may be an important contribution to the pathogenesis of the atheromatous lesions. The next presentation was by Dr. Stephen Katz, who spoke on the involvement of macrophages in skin diseases. He contrasted the characteristics of circulating monocytes and tissue macrophages with the Langerhans cells in the skin and discussed the role of these cell types in a variety of skin diseases. The final presentation was by Dr. Ronald Crystal, who discussed the role of macrophages in chronic inflammatory disorders of the lung, particularly in diseases such as sarcoidosis. From this session, it was clear that macrophages play a central role in both the development of a variety of human diseases and the host resistance against several of these diseases.

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